Public Comments Concerning the Draft NICEATM-ICCVAM 5-Year Plan (2008-2012)

Dr. Catherine Willett
Science Policy Advisor
PETA

Presented at the
Meeting of the NTP Board of Scientific Counselors
June 22, 2007

ICCVAM review of ECVAM-validated methods

Endpoint	Name of Test	ESAC Stmt	ICCVAM Recom.*
Skin corrosion	**EPISKIN™, EpiDerm™, TER**	1998	June 2002
Recommended use only as "positive screens," with *in vitro* negatives subject to "confirmatory" animal testing.			
Pyrogenicity	**5 blood-cell based methods**	March 2006	—
Subject to second peer review in Feb. 2007; report concluded insufficient information for regulatory use of any of the 5 methods. Peer review process was discussed at length at the June 12 SACATM meeting.			
Genotoxicity	***In vitro* micronucleus test**	Nov. 2006	—
Called for substantial additional work prior to acceptance as an OECD Test Guideline.			
Eye corrosion/ severe irritation	**BCOP, ICE**	April 2007	—
Final peer review report published in Nov. 2006; however, final ICCVAM recommendations have yet to be transmitted to federal agencies.			
Skin sensitization	**rLLNA**	April 2007	—
ICCVAM currently proposing a second peer review and other evaluations.			

ESAC-endorsed awaiting ICCVAM review

Endpoint	Name of Test	ESAC Statement
Antibody production	*In vitro* monoclonal antibody production	November 1997
Photoirritation	3T3 neutral red uptake (3T3 NRU) phototoxicity test	May 1998
Vaccine potency	Toxin binding inhibition (ToBI) test	December 2000
Vaccine potency	ELISA test for human tetanus vaccines	December 2000
Embryotoxicity	Embryonic stem cell test (EST)	May 2002
Embryotoxicity	Micromass assay	May 2002
Embryotoxicity	Whole rat embryo assay	May 2002
Vaccine potency	ELISA test for erysipelas vaccines	June 2002
Acute toxicity to fish	Upper threshold concentration (UTC) approach	March 2006
Acute neutropenia	Colony forming unit granulocyte macrophage (CFU-GM) assay	March 2006
Skin corrosion	Skinethic™ human skin model	November 2006
Chronic toxicity	Ending 1-year dog studies of pesticides	November 2006
Skin irritation	EPISKIN™-SIT	April 2007

ICCVAM has put forth 3 test methods that were quickly endorsed by ESAC

Endpoint	Name of Test	ICCVAM Final Recom.	ESAC Stmt.
Skin sensitization	Local lymph node assay	March 1999	October 1999
Acute oral toxicity	Up-and-down procedure (UDP)	March 2000	Not necessary*
Skin corrosion	CORROSITEX™	December 2000	December 2000

* already in use as OECD Test Guideline 425 since September 1998

Any Plan for ICCVAM's future must include an expedited process for reciprocal acceptance of ESAC-endorsed methods

Acute Toxicity

- In 2000, ICCVAM sponsored an international workshop to explore in vitro alternatives to acute toxicity (lethal dose) testing
- Expert consensus
  - cytotoxicity methods were ready for immediate use to set the starting doses
  - “within 2-3 years, if the commitment was strong enough,” they could be put in place as full replacements for these incredibly cruel and outdated animal tests
- Nevertheless, seven years later, ICCVAM is still considering the methods as *possible* reduction measures
- Clearly, commitment in this area is, in fact, absent

ICCVAM must find a way to become proactive and take a lead in method development

Priority Setting

Chapter 1: Priority criteria

1. **Potential impact on reducing, refining, or replacing animals for testing**
2. **Applicability to multiple agencies**
3. **Potential to provide improved prediction of adverse health or environmental effects**

Yet the plan

- **Provides no overview, description or analysis of priority setting for either methods under development or for planned activities**
- **Contains the same laundry list of methods under consideration in November 2006**
- **Does not include suggestions from comments made in December 2006**

Recommended Priorities

- **Ending second-species chronic toxicity and developmental studies**
- ***Moving away from second generation reproductive toxicity studies***
- ***Ending multi-route general toxicity studies***

Any of these would greatly reduce the numbers of animals used

Chronic Toxicity

What the Plan says:

- "NIEHS and FDA continue to seek alternative models that can be used to reduce the number of animals used, shorten the duration of these tests, and provide more accurate predictions of adverse effects.
- However, the development and validation of alternative test methods for this complex endpoint will likely take longer than the five-year time frame for this strategic plan."

- ***These statements do not constitute a plan to deal with these extremely important issues***
- ***The fact that the entire process may be a lengthy one is no excuse for not devising a specific plan to move forward***

Chapter 3: Fostering Acceptance and Appropriate Use of Alternative Test Methods

Opportunity to outline a specific plan for improving regulatory acceptance of validated alternative methods

Would involve

agency input of regulatory endpoints requiring animal testing

specific descriptions of replacement methods

delineation of an integrated validation/regulatory use process

- Instead, the plan:
  - Describes past activities
  - Does not contain an approach to foster acceptance by regulatory agencies
  - Promises “continuing to do” what ICCVAM had been doing

Chapter 4: Developing Partnerships and Strengthening Interactions with ICCVAM Stakeholders

Opportunity to re-strategize, to develop new approaches to improve and strengthen interactions

Yet again, the plan

- Contains descriptions of past activities
- Promises to continue past activities
- Ignores suggestions from solicited comments

These approaches have been demonstrably ineffective for the past decade, and there is no reason to believe they will be more successful in the future

Now more than ever, ICCVAM needs to effectively step up to the plate

Comments

- From the US Animal Protection Community
  - http://iccvam.niehs.nih.gov/pubcomment/5yp_drft_PubCmts.htm, comment #270
- SACATM Working Group
  - Will be posted under the SACATM June 12 meeting minutes when available